Listing of Claims:

1-99 (cancel)

100. (withdrawn) A diversity generation device, comprising

(i) a programmed thermocycler; and,

(ii) a fragmentation module operably coupled to the programmed thermocycler.

101. (withdrawn) The diversity generation device of claim 100, wherein the programmed thermocycler comprises a thermocycler operably coupled to a computer, which computer comprises one or more instruction set, which one or more instruction set does one or more of:

calculates an amount of uracil and an amount of thymidine for use in the programmed thermocycler;

calculates one or more crossover region between two or more parental nucleotides;

calculates an annealing temperature;

calculates an extension temperature; or

selects one or more parental nucleic acid sequence.

102. (withdrawn) The diversity generation device of claim 101, wherein the one or more instruction set receives user input data and sets up one or more cycle to be performed by the programmed thermocycler.

103. (withdrawn) The diversity generation device of claim 102, wherein the input data comprises one or more of: one or more parental nucleic acid sequence, a desired crossover frequency, an extension temperature, or an annealing temperature.

104. (withdrawn) The diversity generation device of claim 101, wherein the one or more instruction set calculates the amount of uracil and the amount of thymidine based on a desired fragment size.

105. (withdrawn) The diversity generation device of claim 103, wherein the one or more instruction set directs the one or more cycle on the diversity generation device, which one or more cycle:

(a) amplifies the one or more parental nucleic acid sequence;

(b) fragments the one or more parental nucleic acid sequence to produce one or more nucleic acid fragment;

(c) reassembles the one or more nucleic acid fragment to produce one or more shuffled nucleic acid; and,

(d) amplifies the one or more shuffled nucleic acid.

106. (withdrawn) The diversity generation device of claim 105, wherein step (a) comprises amplifying the one or more parental nucleic acid sequence in the presence of uracil.

107. (withdrawn) The diversity generation device of claim 105, wherein the one or more cycle pauses between step (a) and step (b) to allow addition of one or more fragmentation reagent.

108. (withdrawn) The diversity generation device of claim 101, wherein the one or more instruction set performs one or more calculation based on one or more theoretical prediction of a nucleic acid melting temperature or on one or more set of empirical data, which empirical data comprises a comparison of one or more nucleic acid melting temperature.

109. (withdrawn) The diversity generation device of claim 105, wherein the one or more instruction set instructs the fragmentation module to fragment the parental nucleic acids to produce one or more nucleic acid fragments having a desired mean fragment size.

110. (withdrawn) The diversity generation device of claim 100, wherein the programmed thermocycler comprises a thermocycler and software for performing one or more shuffling calculations, which software is embodied on a web page or is installed directly in the thermocycler.

111. (withdrawn) The diversity generation device of claim 100, wherein the fragmentation module fragments one or more parental nucleic acids by sonication, DNase II digestion, random primer extension, or uracil incorporation and treatment with one or more uracil cleavage enzyme.

112. (withdrawn) A diversity generation device comprising:

(i) a computer, which computer comprises at least a first instruction set for creating one or more nucleic acid fragment sequence from one or more parental nucleic acid sequence;

(ii) a synthesizer module, which synthesizer module synthesizes the one or more nucleic acid fragment sequence; and,

(iii) a thermocycler, which thermocycler generates one or more diverse sequence from the one or more nucleic acid fragment sequence.

113. (withdrawn) The diversity generation device of claim 112, wherein the first instruction set limits or expands diversity of the one or more nucleic acid fragment sequence by adding or removing one or more amino acid having similar diversity; selecting a frequently used amino acid at one or more specific position; using one or more sequence activity calculation; using a calculated overlap with one or more additional oligonucleotide; based on an amount of degeneracy, or based on a melting temperature.

114. (withdrawn) The diversity generation device of claim 112, wherein the synthesizer module comprises a microarray oligonucleotide synthesizer.

115. (withdrawn) The diversity generation device of claim 114, wherein the synthesizer module comprises an ink-jet printer head based oligonucleotide synthesizer.

116. (withdrawn) The diversity generation device of claim 112, wherein the synthesizer module synthesizes the one or more nucleic acid fragment sequences on a solid support.

117. (withdrawn) The diversity generation device of claim 112, wherein the synthesizer module uses one or more mononucleotide coupling reactions or one or more trinucleotide coupling reactions to synthesize the one or more nucleic acid fragment sequence.

118. (withdrawn) The diversity generation device of claim 112, wherein the thermocycler performs an assembly/rescue PCR reaction.

119. (withdrawn) The diversity generation device of claim 118, wherein the computer comprises at least a second instruction set, which second instruction set determines at least a first set of conditions for the assembly/rescue PCR reaction.

120. (withdrawn) The diversity generation device of claim 112, the device further comprising a screening module for screening the one or more diverse sequence for a desired characteristic.

121. (withdrawn) The diversity generation device of claim 120, wherein the screening module comprises a high-throughput screening module.

122. (withdrawn) A diversity generation kit comprising:

(i) the diversity generation device of claim 100 or claim 112; and,

(ii) one or more reagent for diversity generation.

123. (withdrawn) The diversity generation kit of claim 122, wherein the reagents comprise E coli., a PCR reaction mixture comprising a mixture of uracil and thymidine, one or more uracil cleaving enzyme, and a PCR reaction mixture comprising standard dNTPs.

124. (withdrawn) The diversity generation kit of claim 123, wherein the one or more uracil cleaving enzyme comprises a uracil glycosidase and an endonuclease.

125. (withdrawn) The diversity generation kit of claim 123, wherein the mixture of uracil and thymidine comprises a desired ratio of uracil to thymidine, which desired ratio is calculated by the diversity generation device.

126. (withdrawn) The diversity generation kit of claim 122, wherein the one or more reagents for diversity generation comprise at least a first artificially evolved enzyme.
The diversity generation kit of claim 126, wherein the at least first artificially evolved enzyme comprises an artificially evolved polymerase.

127. (withdrawn) The diversity generation kit of claim 122, further comprising one or more of: packaging materials, a container adapted to receive the device or reagent, or instructional materials for use of the device.

128. (withdrawn) A method of processing shuffled or mutagenized nucleic acids, the method comprising:

(a) providing a physical or logical array of reaction mixtures, a plurality of the reaction mixtures comprising one or more member of a first population of nucleic acids, the first population of nucleic acids comprising one or more shuffled nucleic acids, or one or more transcribed shuffled nucleic acids, or one or more mutagenized nucleic acid or one or more transcribed mutagenized nucleic acids wherein a plurality of the plurality of reaction mixtures further comprise an in vitro translation reactant; and,

(b) detecting one or more in vitro translation products produced by a plurality of members of the physical or logical array of reaction mixtures.

129. (withdrawn) The physical or logical array or reaction mixtures produced by the method of claim 128.

130. (withdrawn) The method of claim 128, wherein the array of reaction mixtures comprises a solid phase or a liquid phase array of one or more of: the one or more shuffled or mutagenized nucleic acids, the one or more transcribed shuffled nucleic acids, or the one or more in vitro translation reagents.

131. (withdrawn) The method of claim 128, wherein the one or more shuffled nucleic acids or the one or more mutagenized nucleic acids are homologous.

132. (withdrawn) The method of claim 128, wherein the one or more transcribed shuffled nucleic acid or the one or more transcribed mutagenized nucleic acid is an mRNA, a catalytic RNA or a biologically active RNA.

133. (withdrawn) The method of claim 128, wherein the one or more in vitro translation reagents comprise one or more of: a reticulocyte lysate, a rabbit reticulocyte lysate, a wheat germ in vitro translation mixture, or an *E coli* lysate.

134. (withdrawn) The method of claim 128, further comprising providing one or more in vitro transcription reagents to the plurality of members of the physical or logical array of reaction mixtures.

135. (withdrawn) The method of claim 134, wherein the in vitro transcription reagents comprises one or more of: a HeLa nuclear extract in vitro transcription component, an SP6 polymerase, a T3 polymerase or a T7 RNA polymerase.

136. (withdrawn) The method of claim 128, wherein the one or more shuffled nucleic acids are produced in an automatic DNA shuffling module, the method comprising inputting DNAs or character strings corresponding to input DNAs into the DNA shuffling module and accepting output DNAs from the DNA shuffling module, which output DNAs comprise the one or more shuffled nucleic acids in the reaction mixture array.

137. (withdrawn) The method of claim 136, comprising fragmenting the input DNA in the DNA shuffling module to produce DNA fragments, or providing the input DNAs to comprise cleaved or synthetic DNA fragments.

138. (withdrawn) The method of claim 136, or 137, comprising purifying DNA fragments of a selected length in the DNA shuffling module.

139. (withdrawn) The method of claim 138, comprising hybridizing the resulting purified DNA fragments and elongating the resulting hybridized DNA fragments with a polymerase.

140. (withdrawn) The method of claim 139, further comprising separating, identifying, cloning or purifying the resulting elongated DNAs.

141. (withdrawn) The method of claim 139, further comprising determining a recombination frequency or a length, or both a recombination frequency and a length for the resulting elongated DNAs.

142. (withdrawn) The method of claim 139, further comprising determining a length of the resulting elongated DNAs by detecting incorporation of one or more labeled nucleic acid or nucleotide into the elongated DNAs.

143. (withdrawn) The method of claim 142, wherein the label is a dye, radioactive label, or a fluorophore.

144. (withdrawn) The method of claim 139, comprising determining the length of the resulting elongated DNAs with a fluorogenic 5' nuclease assay.

145. (withdrawn) The method of claim 139, comprising flowing a shuffling reagent or product through a microscale channel in the DNA shuffling module.

146. (withdrawn) The method of claim 139, wherein the DNA fragments are contacted in a single pool.

147. (withdrawn) The method of claim 139, wherein the DNA fragments are contacted in multiple pools.

148. (withdrawn) The method of claim 139, further comprising dispensing the resulting elongated DNAs into one or more multiwell plates.

149. (withdrawn) The method of claim 139, further comprising dispensing the resulting elongated DNAs into one or more multiwell plates at a selected density per well of the elongated DNAs.

150. (withdrawn) The method of claim 139, further comprising dispensing the resulting elongated DNAs into one or more master multiwell plates and PCR amplifying the resulting master array of elongated nucleic acids to produce an amplified array of elongated nucleic acids, the

shuffling module comprising a array copy system which transfers aliquots from the wells of the one or more master multiwell plates to one or more copy multiwell plates.

151. (withdrawn) The method of claim 150, comprising determining an extent of PCR amplification by one or more technique selected from: incorporation of a label into one or more amplified elongated nucleic acid, and applying a fluorogenic 5' nuclease assay.

152. (withdrawn) The method of claim 150, wherein the array of reaction mixtures is formed by separate or simultaneous addition of an in vitro transcription reagents and an in vitro translation reactant to the one or more copy multiwell plates, or to a duplicate set thereof, wherein the elongated DNAs comprise the one or more shuffled nucleic acids.

153. (withdrawn) The method of claim 128, wherein the array of reaction mixtures produces an array of reaction mixture products.

154. (withdrawn) The method of claim 153, wherein the reaction products comprise one or more polypeptide.

155. (withdrawn) The method of claim 153, wherein the reaction products comprise one or more polypeptide, the method further comprising re-folding the one or more polypeptide by contacting the one or more polypeptide with a refolding reagent.

156. (withdrawn) The method of claim 155, wherein the refolding reagent comprises one or more of: guanidine, urea, DTT, DTE, or a chaperonin.

157. (withdrawn) The method of claim 153, comprising moving the one or more reaction product array members into proximity to a product identification module, or moving a product identification module into proximity to the reaction product array members.

158. (withdrawn) The method of claim 153, wherein the one or more reaction product array members are flowed into proximity to a product identification module, the method further comprising in-line purification of the one or more reaction product array members.

159. (withdrawn) The method of claim 153, further comprising contacting the one or more polypeptide with one or more lipid to produce one or more liposome or micelle, which liposome or micelle comprises the one or more polypeptide.

160. (withdrawn) The method of claim 153, further comprising one or more of:

reading the array of reaction mixture products with an array reader, which reader detects one or more member of the array of reaction products;

converting one or more member of the array of reaction products with an enzyme into one or more detectable products;

converting one or more substrates by the one or more member of the array of reaction products into one or more detectable products;

contacting a cell to one or more member of the array of reaction products, which cell or reaction product, or both, produce a detectable signal upon contacting the one or more member of the array of reaction products;

inducing a reporter gene with one or more member of the array of reaction products;

inducing a promoter with one or more member of the array of reaction products, which promoter directs expression of one or more detectable products; or

inducing an enzyme or receptor cascade with one or more member of the array of reaction products, which cascade is induced by the one or more member of the array of reaction products.

161. (withdrawn) A method of recombining members of a physical or logical array of nucleic acids, the method comprising:

(a) providing at least a first population of nucleic acids, or

(b) providing a data structure comprising character strings corresponding to the first population of nucleic acids;

(c) recombining one or more members of the first population of nucleic acids, thereby providing a first population of recombinant nucleic acids, or

(d) recombining one or more of the character strings corresponding to one or more members of the first population of nucleic acids, thereby providing a population of character strings corresponding to the first population of recombinant nucleic acids, and converting the population of character strings corresponding to the first population of recombinant nucleic acids into the first population of recombinant nucleic acids, thereby providing the first population of recombinant nucleic acids;

(e) spatially or logically separating members of the population of recombinant nucleic acids to produce a physical or logical array of recombinant nucleic acids and amplifying the recombinant nucleic acids in the physical or logical array of recombinant nucleic acids in vitro to provide an amplified physical or logical array of recombinant nucleic acids, or,

(f) in vitro amplifying members of the population of recombinant nucleic acids and physically or logically separating the population of recombinant nucleic acids to produce an amplified physical or logical array of recombinant nucleic acids.

162. (withdrawn) The method of claim 161, further comprising:

(g) screening the amplified physical or logical array of recombinant nucleic acids, or a duplicate thereof, for a desired property.

163. (withdrawn) The method of claim 161, wherein the data structure is embodied in a computer, an analog computer, a digital computer, or a computer readable medium.

164. (withdrawn) The method of claim 161, wherein spatially or logically separating members of the population of recombinant nucleic acids to produce a physical or logical array of recombinant nucleic acids or amplified recombinant nucleic acids comprises plating the nucleic acids in a microtiter tray at an average of approximately 0.1-10 array members per well.

165. (withdrawn) The method of claim 161, wherein spatially or logically separating members of the population of recombinant nucleic acids to produce a physical or logical array of

recombinant nucleic acids comprises plating the nucleic acids in a microtiter tray at an average of approximately 1-5 array members per well.

166. (withdrawn) The method of claim 161, wherein spatially or logically separating the members of the population of recombinant nucleic acids comprises diluting the members of the population with a buffer.

167. (withdrawn) The method of claim 161, wherein the concentration of the population of recombinant nucleic acids is about 0.01 to 100 molecules per microliter.

168. (withdrawn) The method of claim 161, wherein spatially or logically separating members of the population of recombinant nucleic acids to produce a physical or logical array of recombinant nucleic acids comprises one or more of:

(i) lyophilizing members of the population of recombinant nucleic acids on a solid surface, thereby forming a solid phase array;

(ii) chemically coupling members of the population of recombinant nucleic acids to a solid surface, thereby forming a solid phase array;

(iii) rehydrating members of the population of recombinant nucleic acids on a solid surface, thereby forming a liquid phase array;

(iv) cleaving chemically coupled members of the population of recombinant nucleic acids from a solid surface, thereby forming a liquid phase array; or,

(v) accessing one or more physically separated logical array members from one or more sources of recombinant nucleic acids and flowing the physically separated logical array members to one or more destination.

169. (withdrawn) A method of recombining members of a physical or logical array of nucleic acids, the method comprising:

(a) providing at least a first population of nucleic acids arranged in a physical or logical array;

(b) recombining one or more members of the first population of nucleic acids with one or more additional nucleic acid, thereby providing a first physical or logical array comprising a population of recombinant nucleic acids;

(c) amplifying the recombinant nucleic acids in the physical or logical array of recombinant nucleic acids in vitro to provide an amplified physical or logical array of recombinant nucleic acids; and,

(g) screening the first or amplified physical or logical array of recombinant nucleic acids, or a duplicate thereof, for a desired property.

170. (withdrawn) The method of claim 128 or 169, wherein the first population of nucleic acids or the population of recombinant nucleic acids are arranged in a physical or logical matrix at an average of approximately 0.1-10 array members per array position.

171. (withdrawn) The method of claim 128 or 169, wherein the first population of nucleic acids or the population of recombinant nucleic acids are arranged in a physical or logical matrix at an average of approximately 0.5-5 array members per array position.

172. (withdrawn) The method of claim 128 or 169, wherein the first population of nucleic acids or the population of recombinant nucleic acids comprise a solid phase or a liquid phase array.

173. (withdrawn) The method of claim 128 or 169, wherein the first population of nucleic acids is provided by one or more of:

synthesizing a set of overlapping oligonucleotides, cleaving a plurality of homologous nucleic acids to produce a set of cleaved homologous nucleic acids, step PCR of one or more target nucleic acid, uracil incorporation and cleavage during copying of one or more target nucleic acids, and incorporation of a cleavable nucleic acid analogue into a target nucleic acid and cleavage of the resulting target nucleic acid; or,

wherein the set of overlapping oligonucleotides or the set of cleaved homologous nucleic acids are flowed into one or more selected physical locations.

174. (withdrawn) The method of claim 128, 161 or 169, wherein the first population of nucleic acids is provided by synthesizing a set of overlapping oligonucleotides, by cleaving a plurality of homologous nucleic acids to produce a set of cleaved homologous nucleic acids, or both.

175. (withdrawn) The method of claim 128, 161 or 169, wherein the first population of nucleic acids is provided by sonicating, cleaving, partially synthesizing, random primer extending or directed primer extending one or more of: a synthetic nucleic acid, a DNA, an RNA, a DNA analogue, an RNA analogue, a genomic DNA, a cDNA, an mRNA, a DNA generated by reverse transcription, an nRNA, an aptamer, a polysome associated nucleic acid, a cloned nucleic acid, a cloned DNA, a cloned RNA, a plasmid DNA, a phagemid DNA, a viral DNA, a viral RNA, a YAC DNA, a cosmid DNA, a fosmid DNA, a BAC DNA, a P1-mid, a phage DNA, a single-stranded DNA, a double-stranded DNA, a branched DNA, a catalytic nucleic acid, an antisense nucleic acid, an in vitro amplified nucleic acid, a PCR amplified nucleic acid, an LCR amplified nucleic acid, a QƎ-replicase amplified nucleic acid, an oligonucleotide, a nucleic acid fragment, a restriction fragment or a combination thereof.

176. (withdrawn) The method of claim 175, wherein the first population of nucleic acids is further provided by purifying one or more member of the first population of nucleic acids.

177. (withdrawn) The method of claim 128, 161 or 169, wherein the first population of nucleic acids is provided by transporting one or more members of the population from one or more sources of one or more members of the first population to one or more destinations of the one or more members of the first population of nucleic acids.

178. (withdrawn) The method of claim 177, wherein said transporting comprises flowing the one or more members from the source to the destination.

179. (withdrawn) The method of claim 177, the one or more sources of nucleic acids comprising one or more of: a solid phase array, a liquid phase array, a container, a microtiter tray, a

microtiter tray well, a microfluidic chip, a test tube, a centrifugal rotor, a microscope slide, or a combination thereof.

180. (withdrawn) The method of claim 150, 161 or 169, wherein amplifying the recombinant nucleic acids in the physical or logical array of recombinant nucleic acids, or amplifying the elongated nucleic acids in the master array comprises one or more amplification technique selected from: PCR, LCR, SDA, NASBA, TMA and QΞ-replicase amplification.

181. (withdrawn) The method of claim 150, 161 or 169, wherein amplifying the recombinant nucleic acids in the physical or logical array or amplifying the elongated nucleic acids in the master array comprises heating or cooling the physical or logical array or the master array, or a portion thereof.

182. (withdrawn) The method of claim 150, 161 or 169, wherein amplifying the recombinant nucleic acids in the physical or logical array or amplifying the elongated nucleic acids in the master array comprises incorporating one or more transcription or translation control subsequence into one or more of:

the elongated nucleic acids, the recombinant nucleic acids in the physical or logical array, an intermediate nucleic acid produced using the elongated nucleic acids or the recombinant nucleic acids in the physical or logical array as a template, or a partial or complete copy of the elongated nucleic acids or the recombinant nucleic acids in the physical or logical array.

183. (withdrawn) The method of claim 182, wherein the one or more transcription or translation control subsequence is ligated to into one or more of:

the elongated nucleic acids, the recombinant nucleic acids in the physical or logical array, an intermediate nucleic acid produced using the elongated nucleic acids or the recombinant nucleic acids in the physical or logical array as a template, or a partial or complete copy of the elongated nucleic acids or the recombinant nucleic acids in the physical or logical array.

184. (withdrawn) The method of claim 182, wherein the one or more transcription or translation control subsequence is hybridized or partially hybridized to one or more of:

the elongated nucleic acids, the recombinant nucleic acids in the physical or logical array, an intermediate nucleic acid produced using the elongated nucleic acids or the recombinant nucleic acids in the physical or logical array as a template, or a partial or complete copy of the elongated nucleic acids or the recombinant nucleic acids in the physical or logical array.

185. (withdrawn) The method of claim 181, wherein the recombinant nucleic acids in the physical or logical array or the elongated nucleic acids in the master array are amplified in a DNA micro-amplifier.

186. (withdrawn) The method of claim 185, wherein the micro-amplifier comprises one or more of: a programmable resistor, a micromachined zone heating chemical amplifier, a chemical denaturation device, an electrostatic denaturation device, or a microfluidic electrical fluid resistance heating device.

187. (withdrawn) The method of claim 181, wherein the physical or logical array, or portion thereof or the master array or portion thereof, is heated or cooled by one or more of: a Peltier solid state heat pump, a heat pump, a resistive heater, a refrigeration unit, a heat sink, or a Joule Thompson cooling device.

188. (withdrawn) The method of claim 161 or 169, further comprising producing a duplicate amplified physical or logical array of recombinant nucleic acids.

189. (withdrawn) The method of claim 162 or 169, wherein screening the amplified physical or logical array of recombinant nucleic acids, or a duplicate thereof, for a desired property comprises: assaying a protein or product nucleic acid encoded by one or more members of the amplified physical or logical array of recombinant nucleic acids for one or more property.

190. (withdrawn) The method of claim 161 or 169, further comprising in vitro transcribing members of the amplified physical or logical array of recombinant nucleic acids to produce an amplified array of in vitro transcribed nucleic acids.

191. (withdrawn) The method of claim 128 or 169, comprising providing a first population of single-stranded template polynucleotides, which template polynucleotides are the same or different, and recombining the template polynucleotides by:
(i) annealing a plurality of partially overlapping complementary nucleic acid fragments; and,
(ii) extending the annealed fragments to produce a physical or logical array comprising a first population of recombinant nucleic acids.

192. (withdrawn) The method of claim 191, comprising providing a physical array comprising the first population of template polynucleotides immobilized on a solid support.

193. (withdrawn) The method of claim 192, wherein the solid support comprises a glass support, a plastic support, a silicon support, a chip, a bead, a pin, a filter, a membrane, a microtiter plate, or a slide.

194. (withdrawn) The method of claim 192, wherein the first population of template polynucleotides comprises substantially an entire genome.

195. (withdrawn) The method of claim 194, wherein the first population of template polynucleotides comprises a bacterial or fungal genome.

196. (withdrawn) The method of claim 192, wherein the first population of template polynucleotides comprises substantially all of the expression products of a cell, tissue or organism.

197. (withdrawn) The method of claim 196, wherein the first population of template polynucleotides comprises the expression products of a eukaryotic cell, tissue or organism.

198. (withdrawn) The method of claim 192, wherein the first population of template polynucleotides comprises a subset of the expression products of a cell, tissue or organism.

199. (withdrawn) The method of claim 198, wherein the first population of template polynucleotides comprises the expression products of a eukaryotic cell, tissue or organism.

200. (withdrawn) The method of claim 192, the first population of template polynucleotides comprises a library of genomic nucleic acids or cellular expression products.

201. (withdrawn) The method of claim 200, wherein the library of cellular expression products comprises a cDNA library.

202. (withdrawn) The method of claim 191, wherein one or more template polynucleotides comprise one or more of a coding RNA, a coding DNA, an antisense RNA, and antisense DNA, a non-coding RNA, a non-coding DNA, an artificial RNA, an artificial DNA, a synthetic RNA, a synthetic DNA, a substituted RNA, a substituted DNA, a naturally occurring RNA, a naturally occurring DNA, a genomic RNA, a genomic DNA, or a cDNA.

203. (withdrawn) The method of claim 161 or 169, further comprising in vitro transcribing members of the amplified physical or logical array of recombinant nucleic acids to produce an amplified array of transcribed nucleic acids and translating the amplified physical or logical array of transcribed nucleic acids to produce an amplified physical or logical array of polypeptides.

204. (withdrawn) The method of claim 203, further comprising determining a concentration of polypeptide or transcribed nucleic acid at one or more positions in the amplified physical or logical array of polypeptides.

205. (withdrawn) The method of claim 204, further comprising re-arraying the amplified physical or logical array of polypeptides or in vitro transcribed nucleic acids in a secondary polypeptide or in vitro transcribed nucleic acid array which has an approximately uniform concentration of polypeptides or in vitro transcribed nucleic acids at a plurality of locations in the secondary polypeptide array.

206. (withdrawn) The method of claim 204, further comprising determining a correction factor which accounts for variation in polypeptide or in vitro transcribed nucleic acid concentrations

at different positions in the amplified physical or logical array of polypeptides or in vitro transcribed nucleic acids.

207. (withdrawn) The method of claim 203, further comprising adding one or more substrate to a plurality of members of the logical array of polypeptides or in vitro transcribed nucleic acids.

208. (withdrawn) The method of claim 207, further comprising monitoring formation of a product produced by contact between the one or more substrate and one or more of the plurality of members of the logical array of polypeptides.

209. (withdrawn) The method of claim 208, wherein the formation of the product is detected indirectly.

210. (withdrawn) The method of claim 208, wherein the formation of the product is detected by a coupled enzymatic reaction which detects the product or the substrate or a secondary product of the product or substrate.

211. (withdrawn) The method of claim 208, wherein the formation of the product is detected by monitoring peroxide production.

212. (withdrawn) The method of claim 208, wherein the formation of the product is detected directly.

213. (withdrawn) The method of claim 208, wherein the formation of the product is detected by monitoring production or heat or entropy which results from the formation of the product.

214. (withdrawn) The method of claim 203, further comprising selecting the physical or logical array of polypeptides for a desired property, thereby identifying one or more selected member of the physical or logical array of polypeptides which has a desired property, thereby identifying one or more selected member of the amplified physical or logical array of recombinant nucleic acids that encodes the one or more member of the physical or logical array of polypeptides.

215. (withdrawn) The method of claim 214, wherein selecting the physical or logical array is performed in a primary screening assay, the method further comprising one or more of:

(i) re-selecting the one or more selected member of the amplified physical or logical array of recombinant nucleic acids in a secondary screening assay;

(ii) quantifying protein levels at one or more location in the physical or logical array of polypeptides;

(iii) purifying proteins from one or more locations in the physical or logical array of polypeptides;

(iv) normalizing activity levels in the primary screen by compensating for protein quantitation at a plurality of locations in the physical or logical array of polypeptides;

(v) determining a physical characteristic of the one or more selected members; or,

(vi) determining an activity of the one or more selected members.

216. (withdrawn) The method of claim 214, further comprising recombining the one or more selected member of the amplified physical or logical array of recombinant nucleic acids with one or more additional nucleic acids, in vivo, in vitro or in silico.

217. (withdrawn) The method of claim 214, further comprising cloning or sequencing the one or more member of the amplified physical or logical array of recombinant nucleic acids.

218. (withdrawn) The method of claim 161 or 169, further comprising selecting one or more member of the amplified physical or logical array, or a duplicate thereof, based upon the screening of the amplified physical or logical array for a desired property.

219. (withdrawn) The method of claim 218, wherein a plurality of members of the amplified physical or logical array or duplicate thereof are selected, recombined and re-arrayed to form a secondary array of recombined selected nucleic acids, which secondary array is re-screened for the desired property, or for a second desired property.

220. (withdrawn) A method of detecting or enriching for in vitro transcription or translation products, the method comprising:

localizing one or more first nucleic acids which encode one or more moieties proximal to one or more moiety recognition agents which specifically bind the one or more moieties;

in vitro translating or transcribing the one or more nucleic acids, thereby producing the one or more moieties, which one or more moieties diffuse or flow into contact with the one or more moiety recognition agents; and,

permitting binding of the one or more moieties to the one or more moiety recognition agents, and detecting or enriching for the one or more moieties by detecting or collecting one or more material proximal to, within or contiguous with the moiety recognition agent which material comprises at least one of the one or more moieties, which moieties individually comprise one or more in vitro translation or transcription product.

221. (withdrawn) The method of claim 220, further comprising pooling the one or more moieties by pooling the material which is collected.

222. (withdrawn) The method of claim 220, wherein the one or more moieties comprise one or more polypeptides or one or more RNAs.

223. (withdrawn) The method of claim 220, wherein one or more moiety recognition agents comprise one or more antibody or one or more second nucleic acids.

224. (withdrawn) The method of claim 220, wherein the first nucleic acids comprise a related population of shuffled nucleic acids.

225. (withdrawn) The method of claim 220, wherein the first nucleic acids comprise a related population of shuffled nucleic acids, which shuffled nucleic acids encode an epitope tag, which epitope tag is bound by the moiety or the one or more moiety recognition agents.

226. (withdrawn) The method of claim 220, wherein the first nucleic acids comprise a related population of shuffled nucleic acids and a PCR primer binding region, the method further comprising PCR amplifying a set of parental nucleic acids to produce the related population of shuffled nucleic acids.

227. (withdrawn) The method of claim 220, wherein the first nucleic acids comprise a related population of shuffled nucleic acids and a PCR primer binding region, the method further comprising identifying one or more target first nucleic acid by proximity to the moieties which are bound to the one or more moiety recognition agent, and amplifying the target first nucleic acid by hybridizing a PCR primer to the PCR primer binding region and extending the primer with a polymerase.

228. (withdrawn) The method of claim 220, wherein the first nucleic acids comprise an inducible or constitutive heterologous promoter.

229. (withdrawn) The method of claim 220, wherein the first nucleic acids and the one or more moiety recognition agents are localized on a solid substrate.

230. (withdrawn) The solid substrate made by the method of claim 229.

231. (withdrawn) The method of claim 229, wherein the solid substrate is a bead.

232. (withdrawn) The method of claim 229, wherein the first nucleic acids and the one or more moiety recognition agents are localized on the solid substrate by one or more of: a cleavable linker chemical linker, a gel, a colloid, a magnetic field, or an electrical field.

233. (withdrawn) The method of claim 220, further comprising detecting an activity of the moiety or moiety recognition agent.

234. (withdrawn) The method of claim 233, further comprising picking the one or more first nucleic acid with an automated robot.

235. (withdrawn) The method of claim 233, further comprising picking the one or more first nucleic acid by placing a capillary on a region comprising the detected activity of the moiety or moiety recognition agent.

236. (withdrawn) The method of claim 220, wherein the moiety or moiety in contact with the moiety recognition agent cleaves a cleavable linker, which linker attaches the first nucleic acid to a solid substrate.

237. (withdrawn) A method of producing duplicate arrays of shuffled or mutagenized nucleic acids, the method comprising:

providing a physical or logical array of shuffled or mutagenized nucleic acids or transcribed shuffled or transcribed mutagenized nucleic acids; and,

forming a duplicate array of copies of the shuffled or mutagenized nucleic acids or copies of the transcribed shuffled or transcribed mutagenized nucleic acids by physically or logically organizing the copies into a physical or logical array.

238. (withdrawn) The physical or logical array and duplicate array produced by the method of claim 237.

239. (withdrawn) The method of claim 237, wherein the copies are produced by copying the shuffled or mutagenized nucleic acids or transcribed shuffled or transcribed mutagenized nucleic acids using a polymerase or an in vitro nucleic acid synthesizer.

240. (withdrawn) The method of claim 237, further comprising forming an array of reaction mixtures which corresponds to the physical or logical array of shuffled or mutagenized nucleic acids or transcribed shuffled or transcribed mutagenized nucleic acids, which reaction mixtures comprise members of the array of shuffled or mutagenized nucleic acids or transcribed

shuffled or transcribed mutagenized nucleic acids or the duplicate array of copies of the shuffled or mutagenized nucleic acids or copies of the transcribed shuffled or transcribed mutagenized nucleic acids, or a derivative copy thereof.

241. (withdrawn) The method of claim 240, wherein the reaction mixtures further comprise one or more in vitro transcription or translation reagent.

242. (withdrawn) A method of normalizing an array of reaction mixtures, the method comprising:

in vitro transcribing or translating a physical or logical array of shuffled or mutagenized nucleic acids or transcribed shuffled or transcribed mutagenized nucleic acids to produce an array of products; and,

determining a correction factor which accounts for variation in concentration of the products at different sites in the array of products.

243. (withdrawn) The method of claim 242, further comprising producing a secondary product array, which secondary array comprises selected concentrations of the products at one or more sites in the secondary array.

244. (withdrawn) The physical or logical array of shuffled or mutagenized nucleic acids or transcribed shuffled or transcribed mutagenized nucleic acids, the array of products and the secondary array produced by the method of claim 243

245. (withdrawn) The method of claim 243, wherein the secondary array is formed by transferring an aliquot from a plurality of sites in the array of products to a plurality of secondary sites in the secondary array.

246. (withdrawn) The method of claim 245, further comprising diluting the products during said transferring or after transfer to the secondary sites, thereby selecting the concentration of the products at the secondary sites in the secondary array.

247. (withdrawn) A method for recombining one or more nucleic acids, the method comprising:

(a) immobilizing one or more template nucleic acids on a solid support;

(b) annealing a plurality of partially overlapping complementary nucleic acid fragments to the immobilized template nucleic acid;

(c) extending or ligating the annealed fragments to produce at least one heteroduplex, which heteroduplex comprises a template nucleic acid and a substantially full-length heterolog complementary to the template nucleic acid; and,

(d) recovering at least one substantially full-length heterolog.

248. (withdrawn) The method of claim 247, comprising immobilizing a plurality of template nucleic acids on a solid support.

249. (withdrawn) The method of claim 248, wherein the plurality of template nucleic acids comprises substantially an entire genome.

250. (withdrawn) The method of claim 249, wherein the plurality of template nucleic acids comprises a bacterial or fungal genome.

251. (withdrawn) The method of claim 248, wherein the plurality of template nucleic acids comprises substantially all of the expression products of a cell, tissue or organism.

252. (withdrawn) The method of claim 251, wherein the plurality of template nucleic acids comprises the expression products of a eukaryotic cell, tissue or organism.

253. (withdrawn) The method of claim 248, wherein the plurality of template nucleic acids comprises a subset of the expression products of a cell, tissue or organism.

254. (withdrawn) The method of claim 253, wherein the plurality of template nucleic acids comprises the expression products of a eukaryotic cell, tissue or organism.

255. (withdrawn) The method of claim 248, wherein the plurality of template nucleic acids comprises a library of genomic nucleic acids or cellular expression products.

256. (withdrawn) The method of claim 255, wherein the library of cellular expression products comprises a cDNA library.

257. (withdrawn) The method of claim 248, comprising immobilizing the plurality of template nucleic acids in a spatial array.

258. (withdrawn) The method of claim 247, wherein the one or more template nucleic acids comprise one or more of: a DNA, an RNA, a coding RNA, a coding DNA, an antisense RNA, an antisense DNA, a non-coding RNA, a non-coding DNA, an artificial RNA, an artificial DNA, a synthetic RNA, a synthetic DNA, a substituted RNA, a substituted DNA, a naturally occurring RNA, a naturally occurring DNA, a genomic RNA, a genomic DNA, or a cDNA.

259. (withdrawn) The method of claim 247, comprising immobilizing one or more template nucleic acids on a solid support selected from among a glass support, a plastic support, a silicon support, a chip, a bead, a pin, a filter, a membrane, a microtiter plate, and a slide.

260. (withdrawn) The method of claim 247, comprising immobilizing the one or more template nucleic acids by depositing a solution comprising the one or more template nucleic acids on a glass slide, which glass slide is coated with a polycationic polymer.

261. (withdrawn) The method of claim 260, wherein the polycationic polymer comprises polylysine or polyarginine.

262. (withdrawn) The method of claim 259, comprising immobilizing the one or more template nucleic acids by tethering the one or more template nucleic acids to the solid support.

263. (withdrawn) The method of claim 262, wherein tethering comprises chemical tethering, biotin-mediated binding, uv cross-linking, fluorescence activated cross-linking, or heat mediated cross-linking.

264. (withdrawn) The method of claim 247, comprising enzymatically extending the annealed fragments with a DNA or RNA polymerase.

265. (withdrawn) The method of claim 264, comprising enzymatically extending the annealed fragments with a thermostable polymerase.

266. (withdrawn) The method of claim 247, comprising enzymatically extending the annealed fragments with a ligase or nuclease, which ligase or nuclease comprises polymerase activity.

267. (withdrawn) The method of claim 247, comprising extending and ligating the annealed fragments to produce at least one substantially full-length heterolog.
A substantially full-length heterolog produced by the method of claim 247.

268. (withdrawn) An array comprising a plurality of heteroduplexes or full-length heterologs produced by the method of claim 247.

269. (withdrawn) The method of claim 247, comprising recovering the at least one substantially full-length heterolog by

(i) denaturing the heteroduplex;

(ii) annealing at least one oligonucleotide primer to the heterolog; and,

(iii) extending the oligonucleotide primer to produce a duplex polynucleotide.

270. (withdrawn) The method of claim 269, further comprising amplifying the duplex polynucleotide.

271. (withdrawn) The method of claim 270, comprising amplifying the duplex polynucleotide using a boomerang sequence, a splinkerette or a vectorette.

272. (withdrawn) An amplified heterolog produced by the method of claim 270

273. (withdrawn) The method of claim 269, further comprising introducing the duplex polynucleotide into a cell.

274. (withdrawn) The method of claim 273, comprising introducing the duplex polynucleotide into a cell via a vector.

275. (withdrawn) The method of claim 274, wherein the vector is a plasmid, a cosmid, a phage or a transposon.

276. (withdrawn) A vector produced by the method of claim 274.

277. (withdrawn) A cell produced by the method of claim 273.

278. (withdrawn) The method of claim 247, further comprising identifying at least one substantially full-length heterolog with a desired property.

279. (withdrawn) The method of claim 278, comprising identifying the at least one substantially full-length heterolog with a desired property in an automated or partially automated high-throughput assay system.

280. (withdrawn) The method of claim 247, further comprising:

(i) recombining or mutating the at least one substantially full-length heterolog to produce a library of diversified heterologs; and

(ii) optionally, identifying at least one diversified heterolog with a desired property.

281. (withdrawn) A library of diversified heterologs produced by the method of claim 280.

282. (withdrawn) An integrated system comprising an array, which array comprises a plurality of heteroduplexes or full-length heterologs produced by the method of claim 247.

283. (withdrawn) The integrated system of claim 282, further comprising one or more of a detector, a data input device, a data output device, a data storage device, and a controller.

284. (withdrawn) The integrated system of claim 283, wherein the controller comprises one or more of a fluid handling mechanism, an array mobilization mechanism, and an array storage device.

285. (withdrawn) A method of directing nucleic acid fragmentation using a computer, the method comprising: calculating a ratio of uracil to thymidine, which ratio when used in a fragmentation module produces one or more nucleic acid fragment of a selected length.

286. (withdrawn) A method of directing PCR using a computer, the method comprising: calculating one or more crossover region between two or more parental nucleic acid sequence using one or more annealing temperature or extension temperature.

287. (withdrawn) The method of claim 286, comprising calculating the one or more crossover region using one or more theoretical prediction or one or more set of empirical data to calculate a melting temperature.

288. (withdrawn) A method of selecting one or more parental nucleic acids for diversity generation using a computer, the method comprising:

(i) performing an alignment between two or more potential parental nucleic acid sequences;

(ii) calculating a number of mismatches between the alignment;

(iii) calculating a melting temperature for one or more window of w bases in the alignment;

(iv) identifying one or more window of w bases having a melting temperature greater than x;

(v) identifying one or more crossover segment in the alignment, which one or more crossover segment comprises two or more windows having a melting temperature greater than x, which two or more windows are separated by no more than n nucleotides;

(vi) calculating a dispersion of the one or more crossover segments;

(vii) calculating a first score for each alignment based on the number of windows having a melting temperature grater that x, the dispersion, and the number of crossover segments identified;

(viii) calculating a second score based on the number of mismatches, the number of windows having a melting temperature grater that x, the dispersion, and the number of crossover segments identified; and,

(ix) selecting one or more parental nucleic acid based on the first score and/or the second score.

289. (withdrawn) The method of claim 288, further comprising repeating steps (i) through (viii) starting with the one or more parental nucleic acid selected in step (ix).

290. (withdrawn) The method of claim 288, further comprising repeating steps (i) through (viii) starting with the one or more potential parental nucleic acid sequences and one or more different input parameters for calculating the melting temperature in step (ii).

291. (withdrawn) The method of claim 288, wherein the alignment comprises a pairwise alignment.

292. (withdrawn) The method of claim 288, wherein w comprises an odd number.

293. (withdrawn) The method of claim 288, wherein w comprises about 21.

294. (withdrawn) The method of claim 288, further comprising calculating the melting temperature for the one or more window of w bases in the alignment from one or more set of empirical data or one or more melting temperature prediction algorithm.

295. (withdrawn) The method of claim 288, wherein x is about 65 °C.

296. (withdrawn) The method of claim 288, wherein n is about 2.

297. (withdrawn) The method of claim 288, wherein the dispersion comprises the inverse of the average number of bases between crossover segments in the alignment.

298. (withdrawn) The method of claim 288, wherein the instruction set selects the two or more potential parental nucleic acid sequences by searching one or more database for one or more nucleic acid sequence of interest and one or more homolog of the one or more nucleic acid sequence of interest.

299. (withdrawn) A web page for directing nucleic acid diversity generation, the web page comprising a computer readable medium that causes a computer to perform the method of claim 285, claim 286, or claim 288.

300. (previously presented) A system for diversity generation generating diverse nucleic acids, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more target sequences for diversity generation and one or more diverse sequences;

(b) an array;

(c) an automated liquid handler operably coupled to (a) and (b) for dispensing nucleic acids into the array;

(d) a thermocycler operably coupled to the array for generating one or more diverse nucleic acids;

(e) a product production module for automatically generating polypeptide product from the one or more diverse nucleic acids;

(f) a product purification module operably coupled to (e) for purifying the polypeptide product from the product production module, either partially or substantially to homogeneity;

(g) a detector for identifying polypeptide product having a desired property.

301. (previously presented) The system of claim 300, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

302. (previously presented) The system of claim 300, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

303. (previously presented) The system of claim 300, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

304 (previously presented) The system of claim 302, wherein the automated fragmentation module utilizes a reagent selected from the group consisting of a nuclease, a polymerase, a random primer, a directed primer, a nucleic acid cleavage reagent, and a chemical nucleic acid chain terminator.

305. (previously presented) The system of claim 302, further comprising a means for fragment purification.

306. (previously presented) The system of claim 300, wherein the array is a liquid phase array.

307. (previously presented) The system of claim 301, wherein the array is a liquid phase array.

308. (previously presented) The system of claim 302, wherein the array is a liquid phase array.

309. (previously presented) The system of claim 300, further comprising a copy array.

310. (previously presented) The system of claim 300, wherein the product production module conducts in vitro transcription and in vitro translation of the diverse nucleic acids to generate polypeptide product.

311. (previously presented) The system of claim 300, wherein the array is a physical array.

312. (previously presented) The system of claim 311, wherein the array is a microwell plate.

313. (previously presented) The system of claim 300, wherein the array is a logical array.

314. (previously presented) The system of claim 300,

wherein the computer contains data that correspond to one or more diverse sequences, and

wherein the system generates one or more diverse nucleic acids corresponding to the data.

315. (previously presented) The system of claim 301,

wherein the computer contains data that correspond to one or more diverse sequences, and

wherein the system generates one or more diverse nucleic acids corresponding to the data.

316. (previously presented) The system of claim 307,

wherein the computer contains data that correspond to one or more diverse sequences, and

wherein the thermocycler generates one or more diverse nucleic acids corresponding to the data.

317. (previously presented) The system of claim 300, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

318. (previously presented) The system of claim 301, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

319. (previously presented) The system of claim 302, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

320. (previously presented) A system for diversity generation, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more target sequences for diversity generation and one or more diverse sequences;

(b) an array;

(c) an automated liquid handler operably coupled to (a) and (b) for dispensing nucleic acids into the array;

(d) an incubator operably coupled to the array for generating one or more diverse nucleic acids;

(e) a product production module for automatically generating polypeptide product from the one or more diverse nucleic acids;

(f) a product purification module operably coupled to (e) for purifying the polypeptide product from the product production module, either partially or substantially to homogeneity;

(g) a detector for identifying polypeptide product having a desired property.

321. (previously presented) The system of claim 320, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

322. (previously presented) The system of claim 320, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

323. (previously presented) The system of claim 320, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

324. (previously presented) The system of claim 322, wherein the automated fragmentation module utilizes a reagent selected from the group consisting of a nuclease, a polymerase, a random primer, a directed primer, a nucleic acid cleavage reagent, and a chemical nucleic acid chain terminator.

325. (previously presented) The system of claim 322, further comprising a means for fragment purification.

326. (previously presented) The system of claim 320, wherein the array is a liquid phase array.

327. (previously presented) The system of claim 321, wherein the array is a liquid phase array.

328. (previously presented) The system of claim 322, wherein the array is a liquid phase array.

329. (previously presented) The system of claim 320, further comprising a copy array.

330. (previously presented) The system of claim 320, wherein the product production module conducts in vitro transcription and in vitro translation of the diverse nucleic acids to generate polypeptide product.

331. (previously presented) The system of claim 320, wherein the array is a physical array.

332. (previously presented) The system of claim 331, wherein the array is a microwell plate.

333. (previously presented) The system of claim 320, wherein the array is a logical array.

334. (previously presented) The system of claim 320,
wherein the computer contains data that correspond to one or more diverse sequences, and wherein the system generates one or more diverse nucleic acids corresponding to the data.

335. (previously presented) The system of claim 321,
wherein the computer contains data that correspond to one or more diverse sequences, and wherein the system generates one or more diverse nucleic acids corresponding to the data.

336. (previously presented) The system of claim 327,
wherein the computer contains data that correspond to one or more diverse sequences, and wherein the system generates diverse nucleic acids corresponding to the data.

337. (previously presented) The system of claim 320, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

338. (previously presented) The system of claim 321, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

339. (previously presented) The system of claim 322, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

340. (previously presented) A system for diversity generation, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more sequence targets for diversity generation and one or more diverse sequences;

(b) an array;

(c) an automated liquid handler operably coupled to (a) and (b) for dispensing nucleic acids into the array;

(d) a recombination/resynthesis module operably coupled to the array for generating one or more diverse nucleic acids;

(e) a product production module for automatically generating polypeptide product from the diverse nucleic acids;

(f) a product purification module operably coupled to (e) for purifying the polypeptide product from the product production module, either partially or substantially to homogeneity; and

(g) a detector for identifying polypeptide product having a desired property.

341. (previously presented) The system of claim 340, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

342. (previously presented) The system of claim 340, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

343. (previously presented) The system of claim 340, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

344. (previously presented) The system of claim 342, wherein the automated fragmentation module utilizes a reagent selected from the group consisting of a nuclease, a polymerase, a random primer, a directed primer, a nucleic acid cleavage reagent, and a chemical nucleic acid chain terminator.

345. (previously presented) The system of claim 342, further comprising a means for fragment purification.

346. (previously presented) The system of claim 340, wherein the array is a liquid phase array.

347. (previously presented) The system of claim 341, wherein the array is a liquid phase array.

348. (previously presented) The system of claim 342, wherein the array is a liquid phase array.

349. (previously presented) The system of claim 340, further comprising a copy array.

350. (previously presented) The system of claim 340, wherein the product production module conducts in vitro transcription and in vitro translation of the diverse nucleic acids to generate polypeptide product.

351. (previously presented) The system of claim 340, wherein the array is a physical array.

352. (previously presented) The system of claim 351, wherein the array is a microwell plate.

353. (previously presented) The system of claim 340, wherein the array is a logical array.

354. (previously presented) The system of claim 340,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

355. (previously presented) The system of claim 341,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

356. (previously presented) The system of claim 347,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

357. (previously presented) The system of claim 340, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

358. (previously presented) The system of claim 341, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

359. (previously presented) The system of claim 342, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

360. (previously presented) A system for diversity generation generating diverse nucleic acids, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more target sequences for diversity generation and one or more diverse sequences;

(b) an array;

(c) a means for dispensing nucleic acids into the array that is operably coupled to (a);

(d) a means for automatically generating one or more diverse nucleic acids from the nucleic acids in the array;

(e) a means for generating polypeptide product from the diverse nucleic acids that is operably coupled to (d);

(f) a means for purifying the polypeptide product, either partially or substantially to homogeneity, that is operably coupled to (e); and

(g) a means for identifying polypeptide product having a desired property that is operably coupled to (f).

361. (previously presented) The system of claim 360, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

362. (previously presented) The system of claim 360, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

363. (previously presented) The system of claim 360, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

364. (previously presented) The system of claim 362, wherein the automated fragmentation module utilizes a reagent selected from the group consisting of a nuclease, a polymerase, a random primer, a directed primer, a nucleic acid cleavage reagent, and a chemical nucleic acid chain terminator.

365. (previously presented) The system of claim 362, further comprising a means for fragment purification.

366. (previously presented) The system of claim 360, wherein the array is a liquid phase array.

367. (previously presented) The system of claim 361, wherein the array is a liquid phase array.

368. (previously presented) The system of claim 362, wherein the array is a liquid phase array.

369. (previously presented) The system of claim 360, further comprising a means for copying an array.

370. (previously presented) The system of claim 360, further comprising a copy array.

371. (previously presented) The system of claim 360, wherein the product production module conducts in vitro transcription and in vitro translation of the diverse nucleic acids to generate polypeptide product.

372. (previously presented) The system of claim 360, wherein the array is a physical array.

373. (previously presented) The system of claim 372, wherein the array is a microwell plate.

374. (previously presented) The system of claim 360, wherein the array is a logical array.

375. (previously presented) The system of claim 360,
wherein the computer contains data that correspond to one or more diverse sequences, and wherein the system generates one or more diverse nucleic acids corresponding to the data.

376. (previously presented) The system of claim 361,
wherein the computer contains data that correspond to one or more diverse sequences, and wherein the system generates one or more diverse nucleic acids corresponding to the data.

377. (previously presented) The system of claim 367,
wherein the computer contains data that correspond to one or more diverse sequences, and wherein the system generates one or more diverse nucleic acids corresponding to the data.

378. (previously presented) The system of claim 360, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

379. (previously presented) The system of claim 361, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

380. (previously presented) The system of claim 362, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

381. (previously presented) A system for diversity generation generating diverse nucleic acids, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more target sequences for diversity generation and one or more diverse sequences;

(b) an array;

(c) an automated liquid handler operably coupled to (a) and (b) for dispensing nucleic acids into the array;

(d) a thermocycler operably coupled to the array for generating one or more diverse nucleic acids in a liquid phase array;

(e) a product production module for automatically generating polypeptide product from the one or more diverse nucleic acids;

(f) a detector for identifying polypeptide product having a desired property.

382. (previously presented) The system of claim 381, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

383. (previously presented) The system of claim 382, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

384. (previously presented) The system of claim 380, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

385. (previously presented) The system of claim 383, further comprising a means for fragment purification.

386. (previously presented) The system of claim 381,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

387. (previously presented) The system of claim 382,
wherein the computer contains data that correspond to diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

388. (previously presented) The system of claim 381, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

389. (previously presented) The system of claim 382, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

390. (previously presented) The system of claim 383, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

391. (previously presented) A system for diversity generation, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more target sequences for diversity generation and one or more diverse sequences;

(b) an array;

(c) an automated liquid handler operably coupled to (a) and (b) for dispensing nucleic acids into the array;

(d) an incubator operably coupled to the array for generating one or more diverse nucleic acids in a liquid phase array;

(e) a product production module for automatically generating polypeptide product from the one or more diverse nucleic acids;

(f) a detector for identifying polypeptide product having a desired property.

392. (previously presented) The system of claim 391, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

393. (previously presented) The system of claim 391, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

394. (previously presented) The system of claim 390, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

395. (previously presented) The system of claim 393, further comprising a means for fragment purification.

396. (previously presented) The system of claim 391,

wherein the system further comprises a computer containing data that correspond to diverse sequences, and

wherein the system generates one or more diverse nucleic acids corresponding to the data.

397. (previously presented) The system of claim 392,

wherein the system further comprises a computer containing data that correspond to diverse sequences, and

wherein the system generates one or more diverse nucleic acids corresponding to the data.

398. (previously presented) The system of claim 391, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

399. (previously presented) The system of claim 392, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

400. (previously presented) The system of claim 393, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

401. (previously presented) A system for diversity generation, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more target sequences for diversity generation and one or more diverse sequences;

(b) an array;

(c) an automated liquid handler operably coupled to (a) and (b) for dispensing nucleic acids into the array;

(d) a recombination/resynthesis module operably coupled to the array for generating one or more diverse nucleic acids in a liquid phase array;

(e) a product production module operably coupled to (d) for automatically generating polypeptide product from the one or more diverse nucleic acids;

(f) a detector for identifying polypeptide product having a desired property.

402. (previously presented) The system of claim 401, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

403. (previously presented) The system of claim 401, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

404. (previously presented) The system of claim 401, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

405. (previously presented) The system of claim 403, further comprising a means for fragment purification.

406. (previously presented) The system of claim 401,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

407. (previously presented) The system of claim 402,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

408. (previously presented) The system of claim 401, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

409. (previously presented) The system of claim 402, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

410. (previously presented) The system of claim 403, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

411. (previously presented) A system for diversity generation, said system comprising:

(a) a computer containing data that corresponds to one or more sequences selected from the group consisting of one or more target sequences for diversity generation and one or more diverse sequences;

(b) an array;

(c) a means for dispensing nucleic acids into the array that is operably coupled to (a);

(d) a means for generating one or more diverse nucleic acids in a liquid phase array;

(e) a means for generating polypeptide product from the diverse nucleic acids that is operatively coupled to (d); and

(f) a means for identifying polypeptide product having a desired property.

412. (previously presented) The system of claim 411, further comprising an automated oligonucleotide synthesizer operably coupled to (c).

413. (previously presented) The system of claim 411, further comprising an automated fragmentation module operably coupled to (c) for producing fragmented nucleic acids.

414. (previously presented) The system of claim 413, further comprising a means for fragment purification.

415. (previously presented) The system of claim 411, wherein the system generates one or more diverse nucleic acids by assembly of oligonucleotides.

416. (previously presented) The system of claim 411,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

417. (previously presented) The system of claim 412,
wherein the computer contains data that correspond to one or more diverse sequences, and
wherein the system generates one or more diverse nucleic acids corresponding to the data.

418. (previously presented) The system of claim 411, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

419. (previously presented) The system of claim 412, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

420. (previously presented) The system of claim 413, further comprising a second liquid handler for diluting the diverse nucleic acids in an array.

421. (previously presented) The system of claim 300, further comprising a bar-code reader for sample tracking.

422. (previously presented) The system of claim 320, further comprising a bar-code reader for sample tracking.

423. (previously presented) The system of claim 340, further comprising a bar-code reader for sample tracking.

424. (previously presented) The system of claim 360, further comprising a bar-code reader for sample tracking.

425. (previously presented) The system of claim 381, further comprising a bar-code reader for sample tracking.

426. (previously presented) The system of claim 401, further comprising a bar-code reader for sample tracking.

427. (previously presented) The system of claim 411, further comprising a bar-code reader for sample tracking.